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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/721,351	11/26/2003	Wayne D. Comper	62386-043	6164

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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/721,351	COMPER, WAYNE D	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,23 and 25-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,23 and 25-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed January 27, 2006 is acknowledged and entered. Claims 22, 23 and 25-32 are pending and under examination. The numbering of claims is not in accordance with 37 CFR 1.126 because there are two claims that are labeled "claim 28". Misnumbered claims 28-31 been renumbered as 29-32.

2. The following objections and rejection are withdrawn:

- The objection to the specification for failing to update the status of the related applications to which the instant application claims priority is withdrawn in view of Applicant's amendment to the specification.
- The objections to claims 28 and 29 for minor informalities are withdrawn in view of Applicant's amendment.
- The rejection of claim 28 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's amendment.

Claim Rejections - 35 USC § 112

3. The rejection of claims 22-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is moot with regard to cancelled claim 24. The rejection of claims 22, 23 and 25-32 is maintained for reasons of record.

The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The claims are drawn to a method of diagnosing a variety of diseases comprising generating a fragmentation profile for at least one protein from a urine sample obtained from a subject, and comparing said fragmentation profile with a reference fragmentation profile for said at least one protein of a normal individual to determine the presence of disease(s). The specification does not put one of skill in possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the specification only provides partial structure of the proteins (of the fragmentation profile) used to detect the genus of diseases and associated proteins (listed in claims 28 and 31). There is not even identification of any particular portion of the protein structure that must be conserved. The fragmentation profiles (fragment size and sequence) of the various diseases have not been determined in sick or healthy individuals, nor has the specification shown possession of a method of determine the fragmentation profiles. The diseases included in the method are:

Nephropathy
Diabetes insipidus
Diabetes type I
Diabetes type II
Renal disease
Glomerulonephritis
Bacterial glomerulonephritis
Viral glomerulonephritis
IgA nephropathy
Henoch-Schölein Purpura
Membranoproliferative glomerulonephritis
Membranous nephropathy
Sjögren's syndrome
Nephrotic syndrome
Minimal change disease
Focal glomerulosclerosi
Acute renal failure
Acute tumulointerstitial nephritis
Pyelonephritis

GU tract inflammatory disease
Preeclampsia
Renal graft rejection
Leprosy
Reflux nephropathy
Nephrolithiasis
Genetic renal disease
Medullary cystic
Medullary sponge
Polycystic kidney disease
Autosomal dominant polycystic kidney disease
Autosomal recessive plycystic kidney disease
Tuberous sclerosis
Von Hippel-Lindau disease
Familial thin-glomerular basement membrane disease
Collagen III
Glomerulopathy
Fibronectin glomerulopathy
Alport's syndrome
Fabry's disease
Nail-Patella Syndrome
Congenital urologic anomalies
Monoclonal gammopathies
Multiple myeloma
Amyloidosis
Febrile illness
Familial Mediterranean fever
HIV infection- AIDS
Inflammatory disease
Systemic vasculitides
Polyarteritis nodela
Wegener's granulomatosis
Polyarteritis
Necrotizing
Crescentic glomerulonephritis
Polymyositis-dermatomyositis
Pancreatitis
Rheumatoid arthritis
Systemic lupus erythematosus
Gout
Blood disorders
Sickle cell disease
Thrombotic thrombocytopenia purpura
Hemolytic-uremic syndrome
Acute cortical necrosis
Renal thromboembolism
Trauma
Surgery
Extensive injury
Burns
Abdominal and vascular surgery
Induction of anesthesia
Side effect of use of drugs
Drug abuse
Malignant disease
Adenovarcinoma
Melanoma
Lymphoreticular
Multiple myeloma
Circulatory disease
Myocardial infarction
Cardiac failure
Peripheral vascular disease
Atherosclerotic cardiovascular disease
Skin disease
Psoriasis
Systemic sclerosis
Respiratory disease
COPD
Obstructive sleep apnoea
Hypoia at high altitude
Endocrine disease
Acromegaly
Diabetes mellitus

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The specification clearly does not demonstrate possession of fragmentation profiles that diagnose these diseases. One would have to discover and construct profiles for each disease based on age, race, sex, and a number of other factors to determine fragmentation profiles for various individuals. Applicant has not done this work and therefore does not possess the fragmentation profiles that diagnose these diseases in all individuals. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's arguments are primarily drawn to the following:

- Applicant reviews the inventive concept of the instant invention and asserts that there is a shift on the protein fragmentation profile from protein fragments toward an increasing amount of substantially full length protein, and less fragmentation, indicating that the kidneys are not functioning normally to fragment filtered proteins. Applicant points to the specification and the figures for support of their assertion that albumin from healthy individuals, for example, is almost all fragmented, whereas in the profiles of individuals afflicted with renal dysfunction, the size of urinary protein fragments is shifted to larger fragments and the amount of substantially full length protein is significantly increased. Applicant argues that each protein is degraded in a pattern determined by its structure. In the disease individual, the mechanism by which cutting is carried out does not work properly, thus proteins are cut less and in larger fragments.
- Applicant also argues that it is the relative health of the kidneys that affects protein fragmentation, rather than the specific disease causing the kidney dysfunction. The kidneys filter and fragment all proteins indiscriminantly, thus a fragmentation profile from healthy individuals can be obtained for any protein and used as a reference for the protein fragmentation profile obtained from a diseased individual.
  - In response to Applicant's arguments, adequate written description and evidence of possession of a claimed genus remains to be established. While it is within the ability of one of skill in the art to make a fragmentation profile, it is not clear what the cutoff values are for determining whether the individual has renal disease or not. The identity of the intact modified protein that is to be identified is not clear.

While the claims do not specifically recite the term "intact modified", it is critical to understand what intact modified protein looks like in order to compare fragmentation profiled. Applicant indicates that the intact modified protein is similar in molecular weight to normal intact protein, but that there are slight differences that render the protein of a diseased individual different. For example, there may be different epitopes on the proteins of diseased patients that have been filtered improperly through the kidneys. Applicant has not explained what these differences are. Without this information, one of skill in the art would not be put in possession of the instantly claimed method. As a skilled artisan, one would not know what degree of shifting in the spectrophotometer would qualify as indicating renal disease. The specification must provide sufficient distinguishing identifying characteristics of the genus, however, the instant application has not met its burden of providing those identifying characteristics.

4. Claims 22-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is moot with regard to cancelled claim 24. The rejection of claims 22, 23 and 25-32 is maintained for reasons of record.

The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. As outlined above, the claims are drawn to a method of diagnosing a variety of diseases comprising generating a fragmentation profile for at least one protein from a urine sample obtained from a subject, and comparing said fragmentation

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profile with a reference fragmentation profile for said at least one protein of a normal individual to determine the presence of disease(s). The specification does not enable one of skill to practice the claimed invention. There is no guidance for determining the fragmentation profiles of the various diseases in various individuals/groups. There are no working examples of constructing a fragmentation profile for gout, burns, trauma, surgery, etc. The specification fails to teach what kind of proteins and fragments are indicative of what disease(s). Without this knowledge, one of skill cannot diagnose diseases. The specification clearly does not demonstrate enablement of diagnosis because one would have to discover and construct profiles for each disease based on age, race, sex, and a number of other factors to determine fragmentation profiles for various individuals. Applicant has not done this work and therefore has not enabled one of skill to diagnose diseases with the yet-to-be-discovered fragmentation profiles. Therefore, the specification does not enable the practice of the claimed invention for any disease because fragmentation profiles of the "normal" versus "sick" have not been constructed and the specification does not teach how to make the fragmentation profiles that diagnose the diseases listed in claim 28.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's arguments are primarily drawn to the following:

Applicant argues that the particular disease responsible for the kidney dysfunction does not determine the protein fragmentation profile for an individual. Applicant argues that the despite the cause, there is a trend toward larger fragments and substantially full length protein in urine obtained from individuals with renal dysfunction as opposed to the smaller fragmentation of proteins and relative absence of full length protein observed in urine of healthy individuals.

Applicant argues that the specification teaches how to obtain protein fragmentation profiles from both healthy and diseased individuals. The specification also provides examples of profiles from healthy and diseased individuals. Applicant points to the trend toward less fragmentation and more larger fragments, and substantially full length protein in the urine diseased individuals. Thus, Applicant argues that the specification teaches one of skill in the art how to obtain and analyze the fragmentation profile of any individual and make a determination as to whether the profile shows a shift from normal to that of a diseased state indicative of renal dysfunction.

In response to Applicant's arguments, the specification does teach how to obtain fragmentation profiles. But, the specification does not teach how to analyze the fragmentation profiles such that disease can be diagnosed. It is unclear when the shift toward larger and fewer fragments becomes indicative of disease. The Office presumes that identification of the larger or substantially full length protein is referring to intact modified protein disclosed in the specification. While the claims do not specifically recite the term "intact modified", it is critical to understand what intact modified protein looks like in order to compare fragmentation profiled. Applicant indicates that the intact modified protein is similar in molecular weight to normal intact protein, but that there are slight differences that render the protein of a diseased individual different. For example, there may be different epitopes on the proteins of diseased patients that have been filtered improperly through the kidneys. Applicant has not explained what these differences are. Without this information, one of skill in the art would not be capable of practicing the instantly claimed method. It would require undue experimentation to discover what the intact modified proteins of the individual patients looks like and then compare it to the same patient's "normal" intact protein. Applicant has not enabled the diagnosis of renal disease

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or disease/conditions causing renal disease using the claimed method steps. Therefore, the claims remain rejected as lacking sufficient enablement.

Conclusion

5. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Stacy B. Chen 4/5/06

Stacy B. Chen
Primary Examiner
April 5, 2006